

Associated systemic and ocular anomalies in patients with congenital anophthalmos or microphthalmos

Manoj Tyagi¹, Praveen Khare^{2,*}, Meeta Shrivastava³

¹Assistant Professor, ²Associate Professor, ³Professor, Dept. of Ophthalmology, Bundelkhand Medical College Sagar, Madhya Pradesh, India

***Corresponding Author:**

Email: praveenkhare_77@rediffmail.com

Abstract

Congenital anophthalmos and microphthalmos are clinical conditions that result due to abnormalities in development of eye. These conditions may present unilaterally, bilaterally. A large number of these patients have associated systemic anomalies. Patients with unilateral anophthalmos and microphthalmos may present with congenital anomalies of the other eye.

Objective: To document systemic and ocular anomalies in patients with congenital anophthalmos and microphthalmos.

Materials and Methods: Retrospective study of documents of patients present tertiary care center in with congenital anophthalmos and microphthalmos from March 2014-2017. Associated ocular and systemic anomalies were assessed from their records.

Results: Total 42 patients were present during study period. There were 10 (24%) patients with anophthalmos and 32 (76%) were having microphthalmos. 27 were unilateral and 15 bilateral involved. 24 male and 18 female. Mean age of presentation was 9 months. Systemic anomalies were identified in 28% and 66% of unilateral and bilateral anophthalmos. While in microphthalmos systemic involvement was 10% and 30%. Ocular involvement was 40% and 33% in anophthalmos and microphthalmos respectively.

Conclusion: Majority of patients with congenital anophthalmos and microphthalmos have associated systemic and ocular anomalies. We suggest that all patients born with congenital anophthalmos and microphthalmos need complete ophthalmic and systemic examination.

Keywords: Anophthalmos, Microphthalmos, Ocular anomalies, Systemic anomalies.

Introduction

Congenital anophthalmos and microphthalmos are rare anomalies that result from abnormalities in the development of the primary optic vesicle due to various forms of insults to the developing eye/eyes during the first 8 weeks of intrauterine life. They are responsible for significant proportion of childhood blindness worldwide. Prevalence rate for anophthalmos and microphthalmos varies from 0.3, 0.6 per 1000 live birth and 1.4, 1.8, 3.2 per 1000 live birth respectively in several large studies.^(1-4, 9, 10) The term anophthalmos is used when there is no visible ocular remnant. Microphthalmos refers to an eye which is abnormally small in axial length and corneal diameter and may be associated with coloboma or not. It is important to thoroughly examine the patients for associated ocular and systemic anomalies. Some cases may present in syndrome form such as CHARGE syndrome (coloboma, heart defects, choanal atresia, retarded growth and development, genital abnormalities and ear anomalies), or anophthalmos associated with pulmonary hypoplasia.⁽¹³⁾ However most patients present with no syndrome. Congenital anophthalmos and microphthalmos may present unilaterally or bilaterally. Patients with unilateral anophthalmos and microphthalmos may present with congenital anomalies of the other eye such as coloboma, anterior segment and posterior segment abnormalities. A large number of these patients have associated systemic anomalies. The

purpose of our study is to determine the systemic and ocular anomalies in patients with congenital anophthalmos and microphthalmos.

Materials and Methods

We performed a retrospective study of the records of patients which were presented with congenital anophthalmos and microphthalmos between March 2014 till March 2017 in our department. The data of all the patients which were presented was recorded in a self designed performa.

The study was done in department of ophthalmology of tertiary care center in central India. As study was retrospective so no informed consent was obtained from patients parents. Consecutive cases of congenital anophthalmos and microphthalmos were obtained from records.

(Table 1) shows the performa which was used for these patients.

Table 1: Performa for congenital anophthalmos and microphthalmos

Name	Age/Gender
Registration No-	
Mother's Name/Age	
Father's Name/Age	
Address	
Age of Presentation-	
U/L, B/L Anophthalmos/	

Microphthalmos	
Siblings	
Antenatal H/O	
Examination	
Ocular RE/LE	
Fundus	
Systemic Examination- Face/Ear/Palate	
Paediatric Evaluation- Abnormal finding	
Investigation- A Scan/B Scan	
Corneal diameter CT scan /MRI scan (Orbit/ Brain) If required	

Each patient undergoes complete history and thorough ophthalmic examination. The history focuses particularly on any relevant gestational factor or family history of other ocular or systemic abnormalities. The diagnostic assessment confirms anophthalmos, microphthalmos, coloboma or other associated ocular anomalies. Second eye was examined in unilateral cases to detect any subtle abnormalities such as isolated iris coloboma, iris coloboma associates with chorioretinal coloboma, retinal dystrophy, optic nerve hypoplasia, congenital cataract, congenital glaucoma and ocular motility disorders. USG B-scan of eye and orbit was done to determine the internal structures of the eye and to determine the axial length in microphthalmos. Dilated indirect ophthalmoscopy was done to rule out posterior segment abnormalities. Corneal diameter was measured using castrovijo callipers under microscope. Specific attention was focused upon examination of face, ears and palate. Patients were categorized as congenital anophthalmos in which is no evidence of a globe or ocular tissue remnant in the orbit on clinical

examination,⁽¹⁴⁾ while congenital microphthalmia was defined as patient with an abnormally small eye or cornea. Axial length of less than 16mm at birth and 19 mm at 2 years of age and corneal diameter less than 10 mm was considered microphthalmos.⁽¹⁵⁾ Coloboma was defined as deficiency of iris, chorioretinal or optic disc tissue particularly in inferonasal quadrant. Cases were further assessed on the basis of the presence of ocular anomalies (such as coloboma, congenital cataract, congenital glaucoma, posterior segment disorders, naso-larimal and orbital disorders). All patients under goes detailed systemic clinical evaluation. This was performed by paediatrician. Screening for intrauterine infections (TORCH) was done in suspected cases, and further investigations were done according to the systemic anomalies required. Data was analyzed for distribution of anophthalmos and microphthalmos and their association with systemic and ocular anomalies.

Results

A total of 42 patients were present during the study period of 3 years.

Demographic distribution of patients is demonstrated in (Table 2).

The sex distribution of cases was 24 were male and 18 were female. There were 10 (24%) patients with anophthalmos and 32 (76 %) cases were having microphthalmos. There were 27 patients having unilateral involvement and 15 cases have bilateral involvement. In unilateral cases right eye was involved in 15 cases while left was involved in 12 patients. All cases were presented within age group of day 1 to 2 years. Mean age of presentation was 9 months.

Table 2

	No of Patients	Male/Female	RE/LE
U/L Anophthalmos	7	4/3	3/4
B/L Anophthalmos	3	1/2	-
UL Microphthalmos	20	12/8	11/9
B/L Microphthalmos	12	7/5	-

Table 3: Association ocular & systemic anomalies with congenital anophthalmos

	Isolated	Ocular anomalies	Systemic anomalies
CUA (7)	2	3	2
CBA (3)	1	-	2

(Table 3) Demonstrate the ocular and systemic association in patients with anophthalmos. 10 patients were present with anophthalmos. 7 were having unilateral and 3 were having bilateral involvement. Isolated ocular involvement was seen in 3 (30%) patients.

Associated ocular anomalies in unilateral anophthalmos were present in 3 patients (40%). Ocular anomalies

which we got were, 1 case of isolated iris coloboma with congenital cataract, 1 cases of iris coloboma with chorioretinal coloboma, and 1 case of limbal dermoid with nasolacrimal duct block.

Systemic associations were present in 4 (40%) patients. Which were facial defects with pre-auricular tags (1 case), cleft lip & cleft palate with rudimentary ears (1 case), hydrocephalus with facial dysmorphology (1 case), sensorineural deafness with severely delayed milestones (1 case).

Table 4: Association of ocular & systemic anomalies with congenital microphthalmos

	Isolated	Ocular anomalies	Systemic anomalies
CUM (20)	12	6	2
CBM (12)	8	-	4

(Table 4) Demonstrate the systemic and ocular anomalies related with congenital microphthalmos. In our study we have 32 cases of microphthalmos. Isolated ocular involvement was seen in 20 (64%) of patients.

Associated ocular anomalies in unilateral anophthalmos were present in 6 patients (50% of unilateral cases). Ocular anomalies which we got were, 2 cases of isolated iris coloboma, 2 cases of iris coloboma with chorioretinal coloboma, 1 case of congenital cataract and 1 case of blepharophimosis syndrome.

Systemic associations were found in 6 (20%) cases. Distribution of systemic abnormalities found in our study were, 2 cases with cleft lip and palate, 1 case with facial defects (small jaw, nasal deformity), 1 case with hydrocephalus with hearing loss, 1 case with preauricular tags, hemifacial microsomia and rudimentary ears and 1 case with cerebral palsy. Systemic associations were more in cases with bilateral microphthalmos as compared with unilateral cases. Most common systemic anomalies were facial defects followed by neurological defects.

Neurological abnormalities were most frequent in cases with anophthalmos as compared with microphthalmos. Facial anomalies were more frequent in bilateral cases as compared with unilateral cases.

Discussion

The congenital anophthalmos and microphthalmos are rare entities regarding their etiology and prevalence. Various studies have reported that between 40-70% of individuals with either congenital anophthalmos or microphthalmos have associated malformation.^(5,6) The sex distribution was approximately equal in our study as in other similar studies.⁽⁴⁾ In our study of 42 patients we found 40% ocular anomaly and 25% systemic anomalies associated with either congenital anophthalmos or microphthalmos. Anterior segment anomalies were most frequent anomalies in patients with unocular presentation. Congenital cataract and iris coloboma followed by posterior segment anomalies (chorioretinal coloboma, discs coloboma, chorioretinal atrophy and hypoplastic disc. Systemic anomalies were identified in 28% and 66% unilateral and bilateral cases of anophthalmos respectively.

The cause of congenital anophthalmos and microphthalmos are complex and multifactorial. A brief review of embryology is helpful in understanding possible associated anomalies. Optic vesicle formation

occurs at 4 week, optic cup and embryonic fissure formation at the 5 week, and closure of the embryonic fissure at the 6 week. Congenital anophthalmos occurs when there is complete failure of optic vesicle budding or early arrest of its development with subsequent degeneration. Failure of optic vesicle budding may be primary with involvement of ocular tissue only or secondary with complete suppression of forebrain. Congenital microphthalmos results from incomplete invagination of the optic vesicle into the optic cup or defective closure of the embryonic fissure of the optic cup. Disc coloboma occurs from failure of embryonic to meet the optic stalk.⁽⁸⁾ Congenital anophthalmos, microphthalmos and coloboma are likely to be caused by disturbances of the morphological pathway that control eye development, either as a result of primary genetic defect, or external gestational factors, including infections or drugs that can interfere with normal morphogenesis of eye.^(18,19)

During same period when the optic vesicle is forming, the brachial apparatus is also starting to develop and subsequently transform into structures of head and neck. The most appropriate name for the wide phenotypic variation of anomalies which result is the 'Oculo-auricular-vertebral spectrum' (OAVS).^(11,12)

There have been reports of cases which have association with intrauterine infections such as toxoplasma gondii, rubella, cytomegalovirus, herpes simplex virus.^(7-9,16,17)

All patients born with congenital anophthalmos and microphthalmos should go through a thorough pediatric examination for associated congenital anomalies. A coordinated approach with pediatrician is necessary to manage any associated systemic conditions. Genetic diagnosis and investigations can greatly assist in providing a diagnosis and informed genetic counseling.

Conclusion

The development of eye is highly complex process. Normal development of eye is determined by sequential and coordinated expression of eye development genes. Majority of cases have no associated syndrome or chromosomal anomalies, few cases may have associated with syndrome.

These cases of congenital anophthalmos and microphthalmos can have systemic anomalies or ocular anomalies. We suggest that all patients born with congenital anophthalmos and microphthalmos needs thorough ophthalmic and pediatric examination. We found the incidence of associated systemic anomalies in patients with congenital U/L and B/L anophthalmos was 28% and 66% respectively. While incidence of associated systemic anomalies in patients with congenital U/L and B/L microphthalmos was 10% and 30% respectively. In U/L cases of anophthalmos and microphthalmos second eye was involved in 40% and 33% respectively. It is important to reach on overall

diagnosis if possible for management of child. The parent's should we well explained about the prognosis, any visual chances should we take care of. A multidisciplinary approach is required for optimal care of these patients.

19. Morrison D, Fitz Patrick D, Hanson I, et al. National study of microphthalmia, anophthalmia, and coloboma (MAC) in Scotland: investigation of genetic aetiology. *J Med Genet.* 2002;39(1):16-22.

Reference

1. Hornby S J, Gilbert C E, Rahi J K, et al. Regional variation in blindness in children due to microphthalmos, anophthalmos and coloboma. *Ophthalmic Epidemiol.* 2000;7(2):127-138.
2. Bermejo E, Martínez-Frías M-L. Congenital eye malformations: clinical-epidemiological analysis of 1,124,654 consecutive births in Spain. *Am J Med Genet.* 1998;75(5):497-504.
3. Stoll C, Alembik Y, Dott B, Roth M P. Congenital eye malformations in 212,479 consecutive births. *Ann Genet.* 1997;40(2):122-128.
4. Källén B, Tornqvist K. The epidemiology of anophthalmia and microphthalmia in Sweden. *Eur J Epidemiol.* 2005;20(4):345-350.
5. Nakamura K M, Diehl N N, Mohny B G. Incidence, ocular findings, and systemic associations of ocular coloboma: A population-based study. *Arch Ophthalmol.* 2011;129(1):69-74.
6. Tucker S, Jones B, Collin J R O. Systemic anomalies in 77 patients with congenital anophthalmos or microphthalmos. *Eye* 1996;10:310-314.
7. Gregory-Evans C Y, Williams M J, Halford S, Gregory-Evans K. Ocular coloboma: reassessment in the age of molecular neuroscience. *J Med Genet* 2004;41:881-891.
8. Chang L, Blain D, Bertuzzi S, Brooks BP. Uveal coloboma and basic science update. *Curr opin ophthalmol* 2006;17:447-470.
9. Warburg M. Classification of microphthalmos and coloboma. *J Med Genet.* 1993;30(8):664-669.
10. Stoll C, Alembik Y, Dott B, Roth MP. Epidemiology of congenital eye malformations in 131,760 consecutive births. *Ophthalmic paediatr Genet.* 1992;13(3):179-186.
11. Gorlin R J, Pindborg J J, Cohen M M. Syndrome of the dead and neck, 3rd ed. New York: McGraw-Hill, 1989:641.
12. Forrester M B, Merz R D. Descriptive epidemiology of anophthalmia and microphthalmia, Hawaii, 1986-2001. *Birth Defects Res A Clin Mol Teratol.* 2006;76(3):187-192.
13. Vissers L E L M, van Ravenswaaij C M A, Admiraal R, et al. Mutation in a new member of the chromodomain gene family cause CARGE syndrome. *Nat Genet.* 2004;36(9):955-957.
14. Palano G M, Di Pietro M, Scuderi A, Pratico G. Microphthalmia due to congenital varicella infection: a case report. *Minerva pediatri* 2005;57(6):433-439.
15. Kodjikian L, Wallon M, Fleury J, Denis P, Binquet C, Peyron F et al. Ocular manifestation in congenital toxoplasmosis. *Graefes Arch Clin Exp Ophthalmol* 2006; 244(1):14-21.
16. Vermeif-Keers C. Primary congenital aphakia and the rubella syndrome. *Tetralogy* 1975;11(3):257-265.
17. Hutto C, Arvin A, Jacobs R, Steele R, Stagno S, Lyrene R et al. Intrauterine herpes simplex virus infection. *J Pediatr* 1987;110(1):97-101.
18. Shah S P, Taylor A E, Sowden J C, et al; Surveillance of eye Anomalies (SEA-UK) Special Interest Group. Anophthalmos, microphthalmos, and typical coloboma in the United Kingdom: a prospective study of incidence and risk. *Invest Ophthalmol Vis Sci.* 2011;52(1):588-564.